

Appl. No. 10/033,303  
Amdt. dated September 13, 2005  
Reply to Office Action of March 9, 2005 and the Notice of  
Non-Compliant Amendment mailed August 25, 2005

**PATENT**

**REMARKS**

**A. Status of Claims**

Claims 1-3, 6-9, 13-17, 19-21, 25, 26, 67, 68, 71, 73, 80-83, 85, 88, and 112-114 are amended, new claims 115-127 are added, and claims 4, 10-12, 18, 22-24, 27-66, 97-103, and 105-106 are cancelled without prejudice to future prosecution. Therefore, with entry of this amendment, claims 1-3, 5-9, 13-17, 19-21, 25, 26, 67-96, 104, and 107-128 are pending.

**B. Support for Amendments**

Claims 1 and 13 have been amended to clarify that the set of mass/charge ( $m/z$ ) values for monomer sequences is calculated in the claimed method. Support for this amendment can be found, for example, in the specification at page 60 line 29, to page 61, line 5 (stating in part, "As an alternative to storing all the necessary  $m/z$  data (e.g. as data 155), one embodiment of the invention determines the necessary  $m/z$  data on the fly (on an as-needed basis)"); and Figure 14A (351).

Claims 2, 3, 6-9, 14-17, 68, 73, and 80-83 have been amended to clarify that the claimed methods are generally applicable to oligomers (e.g. protein, oligonucleotides, oligosaccharides, lipids and polymers of synthetic origin). Support for these amendments may be found throughout the specification and claims as filed. For example, the specification explicitly states "While the invention is exemplified below with reference to labeled proteins, one of skill in the art will recognize that the labels and labeling methods used are adaptable to the preparation of other labeled oligomers (e.g. oligonucleotides, oligosaccharides, synthetic oligomers, etc." See Applicants Specification at page 30, lines 5-9. See also Example 1 (sequencing of an oligosaccharide), Example 2, (identification of a fatty acid), and Example 12 (DNA sequencing).

Claim 67 has been amended to indicate that the ranking is based on the abundance values and the first abundance parameters as disclosed in original claim 71.

Support for new claims 117, 118, 122, and 123-127 may be found, for example, in the specification at page 23, line 7, to page 24, line 24 (stating in part, "The methods may be practiced by labeling a terminus of a molecule or oligomer with a labeling reagent that incorporates a mass defect and discriminating the resulting mass defect labeled molecules from

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other unlabeled molecules or unlabeled molecule fragments in the mass spectrum ... peaks associated with labeled peptides may be deconvolved from unlabeled peptides by their relative abundance"); page 25 line 25, to page 26, line 11 (stating in part, "Embodiments of the invention may incorporate one or more elements into the label that have a nuclear binding energy (mass defect) that moves the mass of the label to a unique mass position in the spectrum that no other stoichiometric combination of the other elements may have"); page 26, line 32, to page 28, line 17; page 36 line 23, to page 38, line 25 (stating in part, "Defining nuclear binding energies in terms of the  $^{12}\text{C} = 12.000000$  mass standard, preferred elements with unique ion mass signatures are those elements in the periodic table with atomic numbers between 17 (Cl) and 77 (Ir) ... Br and Eu are particularly preferred compounds of the label because they exhibit both two stable isotopes of roughly equal proportions and nuclear binding energies that differ significantly from the periodic peak pattern observed for proteins fragmented in the mass spectrometer"); original claim 100; and Figures 25 and 26. Methods of deconvolution are discussed in detail at page 65, line 14, to page 67, line 4.

Support for new claims 119-122, and 124 may be found, for example, at page 56, line 1, to page 57, line 25 (stating in part, "In another preferred embodiment, for isotopic labels, either natural isotopic abundances or with multiple labels of known relative isotopic abundances, the algorithm may be adapted to qualify or rank the peaks of competing sequences by their conformance to the expected abundances of the isotopic series ... A ranking factor,  $\alpha$ , can be constructed as a transform of mass fragment data (raw or transformed) from two isotopic mass fragments such that ... as the raw count ratio of the isotopic pair approaches the ratio of isotopic abundances, the isotope ranking factor,  $\alpha$ , approached the value or 1"); and Figure 4.

Support for new claim 128 may be found, for example, at page 12, lines 30-32 (stating in part, "fragmenting the labeled oligomer using an enzymatic, chemolytic, or mass spectrometric fragmentation method...").

**C. Response to Restriction Requirement**

In response to the restriction requirement, Applicant elect Group I (claims 1-26, 67-96, and 104-114) for prosecution on the merits. Applicants note that claims 4, 10-12, 18, 22-24, and 105-106 are cancelled with this amendment.

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Applicants further note that claims 115-127 have been added. Claims 115-127 are drawn to machine implemented methods for identifying a labeled oligomer fragment and machine implemented methods for deriving a sequence of at least a portion of an oligomer. As claims 115-127 arise from the same inventive concept as claims 1-3, 5-9, 13-17, 19-21, 25, 26, 67-96, 104, and 107-114, Applicants respectfully request inclusion of new claims 115-127 in Group I for prosecution on the merits.

**D. Provisional Election of Species**

Applicants elect species "a. protein" for initial searching. Applicants note that claims 1-3, 5-9, 13-17, 19-21, 25, 26, 67-84, 107, 108, and 117-121 are generic. Applicants further note that claims 113-116 specifically recite a protein.

Applicants understand that in making this provisional election of species, the Examiner will, as a preliminary matter, search the single species provisionally elected above. If no prior art is found that anticipates or renders obvious the provisionally elected species, Applicants expect the search to be extended "to the extent necessary to determine the patentability" of the claim. MPEP §803.02. In as much as the Examiner's election requirement is not intended to be a provisional election of species under MPEP §803.02, Applicants respectfully traverse as an improper attempt to restrict species within a Markush group.

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**CONCLUSION**

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858-350-6100.

Respectfully submitted,



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